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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,616	05/16/2001	Hans-Ulrich Bernard	REF/BERNARD	6676

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EXAMINER
KWON, BRIAN YONG S

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/763,616	Applicant(s) BERNARD ET AL.	
	Examiner Brian S Kwon	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,14,17-20,23-35 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14,17-20,23-35 and 40* is/are rejected.

7)☒ Claim(s) *22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Sequence Rules Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). See Figure 1 and page 4, line 4; page 7, line 29; page 9, line 18; However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant is given ONE MONTH, or THIRTY DAYS, whichever is longer, from the mailing date of this letter within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Status of Application

1. Acknowledgement is made of applicants election of the Group II, without traverse, along with Compound 16 as the elected species. Claims 13, 14, 17-20, 23-35 and 40 are readable on the elected species.

2. By Amendment filed December 5, 2002, Claims 1-12, 36 and 39 have been cancelled and Claim 40 has been amended. Claims 13, 14, 17-20, 23-35 and 40 are currently pending for the prosecution on the merits.

Claim Objections

3. Claim 22 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The scope of claimed substituent in claim 22 is broader than the claimed substituent in claim 21.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 40 is rejected under 35 USC 112, first paragraph, because the specification while being enabling for the specific compounds represented by formula (I) having at least 30% zinc release in a TSQ assay and the activity of inhibiting or reducing the binding of an E6 protein to E6AP or E6BP and cytotoxic effects on HPV containing cell lines, does not reasonably provide enablement for the term "a compound capable of facilitating the disruption of a chelated metal cation domain of protein encoded for by an MPV gene to a mammal in need thereof". The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicants fails to provide information allowing the skilled artisan to ascertain "a compound capable of facilitating the disruption of a chelated metal cation domain of protein encoded for by an MPV gene" without undue experimentation. The instant claims read on all "a compound capable of facilitating the disruption of a chelated metal cation domain of protein encoded for by an MPV gene", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ 1400 (CAFC 1988) at 1404 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls) at 547 the court recited eight factors:

1) the quality of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working example,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

5. Claims 13, 14, 17-20, 23-35 and 40 rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The present claim is drawn to a method of treating or preventing a disease condition caused by exacerbated by an MPV comprising administering a compound capable of facilitating the disruption of a chelated metal cation domain of a protein encoded for by an MPV gene, namely compounds of formula (I) or (II).

The instant specification discloses that the claimed disease conditions include cervical cancer, precursor lesions of this malignant neoplsia which are called cervical intraepithelial neoplasia (CIN) or squamous intraepithelial lesions (SIL), genital warts and common warts and plantar warts which are commonly caused by HPV (page 1, line 25 thru page 2, line 1; page 6, lines 17-28). Furthermore, the instant specification refers to Table 1 of page 37 of Human Papillomarviruses [Volumne 65 (1995) IARC Monographs on the evolution of carcinogenic risks in Humans, The International Agency for Research on Cancer, World Health Organisation, IARC, Lyon, France} as the claimed disease conditions that may be treated in accordance with the present invention (page 7, lines 5-9).

The instant invention is based on studies regarding (i) the activity of the specific compounds represented by formula (I) or (II), namely C16, which have been identified by TSQ assay and assay of measuring the ability of the compound to inhibit the binding of the E6 protein to E6AP or E6BP, in killing HPV containing cell lines as HeLa, SiHa and Caski (Examples 2-5),

specifically HPV16-positive and HPV18-positive cell lines. The instant specification provides sufficient information regarding the activity of C16, having at least 30% zinc release in TSQ assay and the activity of inhibiting the binding of the E6 protein to E6AP or E6BP, in inhibiting growth of HPV16-postive and HPV18-positive cervical tumor cell lines. However, the instant specification (Tables 1-3) fails to provide adequate written description for whether all the compounds represented by formula (I) or (II) which have been identified by TSQ assay (at least 30% zinc release) and assay of measuring the ability of the compound to inhibit the binding of the E6 protein to E6AP or E6BP would have the cytotoxic effects on HPV containing cell lines, namely HPV16-positive and HPV18-positive cell lines. In fact, for example, R25 does not show any cytotoxic effects (also, C27 and R24 do not show any specific cytotoxic effects).

The specification do not clearly provide an adequate representation regarding (i) whether all the claimed compounds represented by formula (I) or (II) that are identified by TSQ assay and assay of measuring the ability of the compound to inhibit the binding of the E6 protein to E6AP or E6BP, are effective in inhibiting the growth of HPV16-postive and HPV18-positive cervical tumor cell lines; (ii) whether the claimed compounds capable of facilitating the disruption of two Cys-X2-Cys-X29-Cys-X2-Cys zinc fingers of HPV E6 and E7 are effective in inhibiting growth of other HPV containing cell lines (other than HPV16-positive and HPV18-positive cell lines); and (iii) the conclusion of the claimed method of treating or preventing said disease in animal from in-vitro study of using C16 in inhibiting growth of HPV16-postive and HPV18-positive cervical tumor cell lines. In addition, the specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of inhibiting of growth of HPV16-postive and HPV18-positive cervical tumor cell lines (in-vitro), the skilled artisan cannot envision the claimed method of treating said disease conditions in animal nor the method of inhibiting the growth of non-HPV16-positive or non-HPV18-positive cell lines. Furthermore, the skilled artisan cannot envision the claimed method of preventing said disease condition in animal. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614,*

1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.*

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim 23 is unclear what is meant by "at least one of R1-R4 is as depicted in any compound in Groups 1 to 6 as defined herein." Furthermore, Claim 23 lacks antecedent basis for "in Groups 1 to 6 as defined herein" in claim 13.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 40 is rejected under 35 U.S.C. 102(b) as being anticipated by Tran et al. (Cancer Reasearch 55, 4599-4605, October 15, 1995).

Tran teaches the use of antisense ODNs in inhibiting tumors caused by MPV (page 4601, column 2, lines 22-25; page 4604, column 2, lines 4-6).

Although the reference is silent about "capable of facilitating the disruption of a chelated metal cation domain of a protein encoded for by an MPV gene", "contacting a protein molecule containing a chelated metal cation domain, encoded by an MPV gene", and "facilitate disruption of the chelated metal cation domain and directly or indirectly determining the amount of chelated metal cation released wherein the amount of chelated metal cation released is indicative of the disruption of the chelated metal cation domain", such recitations of inherent properties are not limiting to the interpretation. Thus, the reference anticipates the claimed invention.

8. Claims 13-15, 20, 31, 32, 33 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Rotstein et al. (Carcinogenesis, 1988, 9(9), 1547-51).

Rotstein teaches the use of disulfiram (a compound of formula (II)) for treating or preventing cancer by treating papillomas, which are population of putative precancerous lesions.

Although Rotstein is silent about (i) "a compound capable of facilitating the disruption of a chelated metal cation domain of a protein encoded for by an MPV gene" in claim 13; "the chelated metal cation domain is a chelated zinc cation domain" in claims 31 and 40; "the chelated zinc is the sequence motif cys-X2-cys-X29-cys-X2-cys" in claim 32; and "facilitate disruption of the chelated metal cation domain and directly or indirectly determining the amount of chelated metal cation released wherein the amount of chelated metal cation released is indicative of the disruption of the chelated metal cation domain" in claim 40, such recitations of

inherent properties are not limiting to the interpretation. Thus, the reference anticipates the claimed invention.

Conclusion

9. No Claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703)308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600